

Senate Testimony
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Thank you, Senators, for the opportunity to testify.

Let me start first with some comments on how dangerous COVID-19 is at an individual level. Early in the epidemic, the World Health Organization publicized a very misleading 3.4% case fatality rate that panicked the world. This number is misleading because, for the typical person infected, the usual outcome spans the range from no symptoms whatsoever, to a mild cold, to the severe viral pneumonia that the media highlights.

Thus, many infections are not identified as cases because they do not come to the attention of doctors or public health authorities. We know from a series of studies of specific SARS-CoV-2 antibodies in the blood, which provide evidence of prior COVID infection, that this is true. From these studies, we can estimate the true COVID infection survival rate.

Because of a recent publication in the Bulletin of the World Health Organization, surveying 61 of these studies worldwide, we now have a good estimate of the infection survival rate. It turns out to vary by orders of magnitude by age. For people 70 and over, the infection survival rate is 95%. For people under 70, it is 99.95%.¹ With improvements in treatment and patient management – like dexamethasone and improved ventilator protocols – these numbers are improving all the time.

At the same time, the harms of the lockdown are manifold and devastating, including plummeting childhood vaccination rates², worse cardiovascular disease outcomes³, less cancer screening⁴, and deteriorating mental health⁵, to name a few. The toll is already high, and it will get worse in coming years,

¹ Ioannidis JP (2020) Infection Fatality Rate of COVID-19 Inferred from Seroprevalence Data. *Bulletin of the World Health Organization*. Article ID: BLT.20.265892. https://www.who.int/bulletin/online_first/BLT.20.265892.pdf

² CDC (2020) Effects of the COVID-19 Pandemic on Routine Pediatric Vaccine Ordering and Administration — United States, 2020. *MMWR*. 69(19): 591-3. <https://www.cdc.gov/mmwr/volumes/69/wr/mm6919e2.htm>

³ Ball S, Banerjee A, Berry C, et al Monitoring indirect impact of COVID-19 pandemic on services for cardiovascular diseases in the UKHeart Published Online First: 05 October 2020. doi: 10.1136/heartjnl-2020-317870

⁴ Rutter MD, Brookes M, Lee TJ, et al Impact of the COVID-19 pandemic on UK endoscopic activity and cancer detection: a National Endoscopy Database Analysis Gut Published Online First: 20 July 2020. doi: 10.1136/gutjnl-2020-322179

⁵ Vizard T, Davis J, White E, Beynon B (2020) Coronavirus and depression in adults, Great Britain: June 2020. Office for National Statistics, UK.

as more people come in with late-stage cancer, worsening diabetes, and advanced heart disease that should have been identified and treated this year.

The social isolation induced by lockdown has led to a sharp rise in opioid and drug-related overdoses⁶, similar to the “deaths of despair” that occurred in the wake of the 2008 Great Recession.⁷ Social isolation of the elderly has contributed to a sharp rise in dementia-related deaths around the country.⁸ For children, the cessation of in-person schooling since the spring has led to “catastrophic” learning losses⁹, with severe projected adverse consequences for affected students’ life spans.¹⁰ According to a CDC estimate, one in four young adults seriously considered suicide this past June.¹¹ Among 25 to 44-year olds, the CDC reports a 26% increase in excess all-cause mortality relative to past years, though fewer than 5% of 2020 deaths have been due to COVID-19.^{12, 13}

The two main planks of focused protection and the Great Barrington Declaration follow logically from these two facts. For older people, COVID-19 is a deadly disease that should be met with overwhelming resources aimed at protecting them wherever they are, whether in nursing homes, at their own home, in the workplace, or multi-generational homes. They should be prioritized for vaccines, and we should be actively seeking widely available and effective treatments. For the

<https://www.ons.gov.uk/peoplepopulationandcommunity/wellbeing/articles/coronavirusanddepressioninadultsgr eatbritain/june2020>

⁶ American Medical Association (2020) Issue Brief: Reports of Increases in Opioid- and Other Drug Related Overdose and Other Concerns During COVID Pandemic. AMA Advocacy Resource Center. Oct. 31, 2020. <https://www.ama-assn.org/system/files/2020-11/issue-brief-increases-in-opioid-related-overdose.pdf>

⁷ Deaton A and Case A (2020) Deaths of Despair and the Future of Capitalism. Princeton University Press. March 17, 2020.

⁸ Alzheimer’s Impact Movement (2020) The 2020 COVID-19 Pandemic and Dementia: Deaths Above Average. <https://www.scribd.com/document/483085777/Dementia-Deaths-Above-Average-State-by-State-Table>

⁹ Center for Research on Education Outcomes (2020) Estimates of Learning Loss in the 2019-2020 School Year. CREO Stanford University. October 2020.

https://credo.stanford.edu/sites/g/files/sbiybj6481/f/short_brief_on_learning_loss_final_v.3.pdf

¹⁰ Christakis DA, Van Cleve W, Zimmerman FJ. Estimation of US Children’s Educational Attainment and Years of Life Lost Associated With Primary School Closures During the Coronavirus Disease 2019 Pandemic. *JAMA Netw Open*. 2020;3(11):e2028786. doi:10.1001/jamanetworkopen.2020.28786

¹¹ Czeisler MÉ, Lane RI, Petrosky E, et al. Mental Health, Substance Use, and Suicidal Ideation During the COVID-19 Pandemic — United States, June 24–30, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:1049–1057. DOI: <http://dx.doi.org/10.15585/mmwr.mm6932a1>

¹² Rossen LM, Branum AM, Ahmad FB, Sutton P, Anderson RN. Excess Deaths Associated with COVID-19, by Age and Race and Ethnicity — United States, January 26–October 3, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:1522–1527. DOI: <http://dx.doi.org/10.15585/mmwr.mm6942e2>

¹³ CDC (2020) Provisional COVID-19 Death Counts by Sex, Age, and State. <https://data.cdc.gov/NCHS/Provisional-COVID-19-Death-Counts-by-Sex-Age-and-S/9bhg-hcku>

non-vulnerable, who face far greater harm from the lockdowns than they do from COVID-19 infection risk, the lockdowns should be lifted and – for those who so decide – normal life resumed.

But what about better treatments for COVID-19 patients? I said earlier that we have made a lot of progress in learning how to manage and treat the disease over the past months, but I think it has been a lot less than it should have been. Strikingly, the most useful advance in treatment involves the repurposing of a drug that is already in widespread use and entirely off patent – the steroid dexamethasone, which is effective in helping severely ill COVID patients avoid a deadly and detrimental immune response.

As a professor of medicine, my inbox is filled with scientists and physicians who have ideas for similarly repurposing existing drugs, vitamins and minerals, and other therapies for the early treatment of COVID-19 infection. For many of these ideas, there are good pathophysiological reasons and observational evidence to believe that they might work.¹⁴ However, there are typically no randomized trials to evaluate whether they work. Doctors are free to use them off-label (that is, the FDA approved their use in the past for some other indication), but they lack a gold standard evaluation of the efficacy in the outpatient management of COVID-19, so most will not do so.

Before dismissing these treatments as ineffective because of lack of randomized evidence, I think the question we need to answer is – why have there been so few randomized evaluations of these therapies? For the answer, I am going to put on my economist's hat.

For drugs and therapies on patent, a patent holder has a strong interest in running randomized evaluations and navigating the drug through the FDA's approval process. By contrast, for drugs and therapies with no patent holder, no one has much interest in funding expensive randomized

¹⁴ McCullough, Peter A et al. "Pathophysiological Basis and Rationale for Early Outpatient Treatment of SARS-CoV-2 (COVID-19) Infection." *The American journal of medicine*, S0002-9343(20)30673-2. 7 Aug. 2020, doi:10.1016/j.amjmed.2020.07.003

trials or working assiduously to move through the FDA regulatory process for rapid approval (or even slow approval).

The bottleneck then is not the FDA.¹⁵ It is the lack of a residual claimant for these drugs and treatment. Investigators working at academic medical centers may have a reputational interest in evaluating these drugs and therapies. But they must find funds from somewhere for them, and pharmaceutical companies typically have no interest in it.

In principle, the NIH exists to solve this market failure. It could and should use its resources to help fund randomized evaluations of these drugs for off-label purposes. And it has funded some important drug evaluation work, such as a study to determine the right dosage and metabolism of drugs prescribed to children with COVID-19.¹⁶ The NIH has also funded some small trials, such as one for Acalabrutinib for hospitalized COVID-19 patients, but that drug is on patent.¹⁷

The NIH has made comparatively little effort to catalyze randomized evaluations of off-patent drugs for COVID-19 therapeutics. By contrast, the NIH has devoted considerable resources to aid the COVID-19 vaccine randomized trial studies.¹⁸ Even the highest-profile randomized evaluation of dexamethasone was not funded by the NIH.¹⁹ The NIH's relative lack of interest in the rapid randomized evaluation of non-patented drug evaluation represents a government failure that has likely led to worse COVID-19 outcomes than we would have had otherwise.

¹⁵ Rome BN, Avorn J. Drug Evaluation during the Covid-19 Pandemic. *N Engl J Med*. 2020 Jun 11;382(24):2282-2284. doi: 10.1056/NEJMp2009457. Epub 2020 Apr 14. PMID: 32289216.

¹⁶ National Institutes of Health Press Release (2020) NIH-Funded Study to Evaluate Drugs Prescribed to Children with COVID-19. <https://www.nih.gov/news-events/news-releases/nih-funded-study-evaluate-drugs-prescribed-children-covid-19>

¹⁷ National Institutes of Health Press Release (2020) Cancer drug may reduce symptoms of severe COVID-19. <https://www.nih.gov/news-events/nih-research-matters/cancer-drug-may-reduce-symptoms-severe-covid-19>

¹⁸ National Institutes of Health Press Release (2020) Promising Interim Results from Clinical Trial of NIH-Moderna COVID-19 Vaccine. <https://www.nih.gov/news-events/news-releases/promising-interim-results-clinical-trial-nih-moderna-covid-19-vaccine>

¹⁹ RECOVERY Collaborative Group (2020) Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report. *New England Journal of Medicine*. July 17, 2020. DOI: 10.1056/NEJMoa2021436